Docket No.: 532212000623
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Thomas L. CANTOR et al.

Application No.: 10/617,489 | Confirmation No.: 4476

Filed: July 10, 2003 | Art Unit: 1641

For: METHODS, KITS AND ANTIBODIES FOR DETECTING PARATHYROID HORMONE | Examiner: C. Cheu

STATEMENT OF SUBSTANCE OF INTERVIEW

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

On February 19th, 21st and 22nd, 2008, Examiner Jacob Cheu and the undersigned had telephonic interviews to discuss the various outstanding issues for the present application. Applicants and the undersigned greatly appreciate Examiner Cheu for granting the interviews and discussing the various issues with the undersigned. The following is a summary of the February 19th, 21st and 22nd, 2008 interviews.

The Examiner and the undersigned discussed the contents of Declaration of John W. Colford, M.D. in Opposition to Plaintiff's Motion for Partial Summary Judgment on Defendants' Counterclaim of Patent Invalidity Under 35 U.S.C. §§102 and 103, filed December 17, 2007 (Colford Declaration) and its two exhibits:

Exhibit A. Colford J, Salvati M, MacFarlane G, Sokoll L, and Levine M. , entitled "Isolation and Characterization of Large Molecular Weight Fragments of PTH," #P3-194 79th Annual Meeting of the Endocrine Society Program and Abstracts, Minneapolis, MN, June 11-14,

1997, including the Abstract #P3-194 (pages 1 and 2 of 18) and additional presentation material (pages 3-18 of 18) (Colford 1997 Abstract and Presentation); and

Exhibit B. Colford J, Salvati M, Hawkins D.M., Sokoll L.J., Udelsman R. and Levine M.A., entitled "Isolation and Characterization and Preliminary Clinical Utility of Two Novel Parathyroid Hormone Molecular Forms." The Exhibit B itself does not contain any publication information but Colford stated in his declaration that he "had prepared and circulated" Exhibit B. (Colford Declaration, paragraph 5 at page 2.)

Colford Declaration and its exhibits were submitted by Immutopics in the *Scantibodies Laboratory, Inc. v. Immutopics, Inc.*, currently pending in the United States District Court for the Central District of California, Case No. CV 04-08871 MRP (MANx). Applicants submitted Colford Declaration with its exhibits and Immutopics' Memorandum of Points and Authorities in Opposition to Plaintiff's Motion for Partial Summary Judgment on Defendants' Counterclaim of Patent Invalidity Under 35 U.S.C. §§102 and 103, filed December 17, 2007 in a Supplemental Information Disclosure Statement in connection with the present application on February 1, 2008. As part of the telephonic interviews on February 19th, 21st and 22nd, 2008, the undersigned sent a courtesy copy of R. LePage et al., "A non-(1-84) circulating parathyroid hormone (PTH) fragment interferes significantly with intact PTH commercial assay measurements in uremic samples," Clin Chem (1998); 44: 805-810 (LePage article) to the Examiner and discussed the content of the LePage article.

The Examiner and the undersigned discussed the data shown at page 12 of Exhibit A (or Exhibit A Page 9 of 18) of Colford Declaration and the illustrations shown at page 13 of Exhibit A (or Exhibit A Page 10 of 18). The undersigned pointed out that the data at page 12 of Exhibit A show some detection of PTH β peak by the "PTH (1-7)" antibody. The undersigned also pointed out that there is no conclusive evidence in Colford Declaration or its Exhibits A and B to show what "PTH α" and "PTH β" forms are.

The undersigned brought to the Examiner's attention paragraph 8 of Colford Declaration, which states that the "PTH (1-7) antibody" was "derived from the antisera of goats that

had been immunized with a fragment of PTH, namely, PTH (1-34)" and the "antisera was affinity purified utilizing an N-terminal segment of PTH, namely PTH (1-13) which represents the first 13 amino acids of the N-terminal of the whole PTH (1-84) molecule." (*See* Colford Declaration, paragraph 8 at page 3.)

The undersigned pointed out that other than Colford's statement in his declaration that he "had prepared and circulated" Exhibit B, there is no evidence that Exhibit B of Colford Declaration has been published. The undersigned also pointed out that Colford's statement alone that he "had prepared and circulated" Exhibit B does not establish that Exhibit B has been published. The undersigned further pointed out that, to the extent that the Examiner is going to consider the disclosure of Exhibit B of Colford Declaration, the Examiner needs to decide the threshold question, on the currently available evidence, whether Exhibit B or its disclosure qualifies as prior art to the present application. The undersigned stated that the applicants reserve the rights to respond to the Examiner's decision on this threshold question and on the Examiner's interpretation of Colford Declaration and its Exhibits A and B.

The undersigned brought to the Examiner's attention the following paragraph from Exhibit B of Colford Declaration:

> An "in-house" IRMA tracer was prepared by purification of a polyclonal goat antiserum against N-terminal hPTH on a Sulfo-link® (Pierce, Rockford, IL) affinity matrix column to which hPTH (1-13-cys) (Synpep, Dublin, CA) peptide had been conjugated through the cysteine. The tracer was validated using (1-84) and (7-84) recognition studies which clearly showed no cross-reactivity to synthetic PTH (7-84), while maintaining the linearity, recovery, and precision characteristics of the commercial DiaSorin intact PTH assay.

(*See* Exhibit B of Colford Declaration at page 27 (or Exhibit B Page 6 of 33).) The undersigned pointed out that the undersigned could not find any experimental data, in Colford Declaration or its Exhibits A and B, to support the statement that the "in-house" IRMA tracer "showed no cross-reactivity to synthetic PTH (7-84)."

The Examiner and the undersigned discussed the data shown at pages 40-41 of Exhibit B of Colford Declaration (or Exhibit B Page 19 of 33 to 20 of 33)), which show comparisons of PTH test results on CFR samples using four different PTH assays: "DSL," "Nicho," "DiaSorin" and "(1-7)." The undersigned pointed out that for almost all the samples tested, the "(1-7)" assay gives signal readouts that are higher than or comparable to the signal readouts detected by the "DiaSorin" assay.

The Examiner and the undersigned also discussed the data shown in Figure 5, at page 45 of Exhibit B of Colford Declaration (or Exhibit B Page 24 of 33). The undersigned pointed out that the "(1-7)" assay gives signal readout that is higher than or comparable to the signal readout detected by the "DiaSorin" assay with respect to the "PTH β" form.

The undersigned pointed out that the above data indicate that the "(1-7)" assay correlates with the "DiaSorin" assay. The undersigned pointed out that this correlation was recognized in Exhibit B of Colford Declaration as well, which states that the "immunoassay value differences between the DiaSorin and "in-House" IRMA with a tracer that does not report PTH (7-84) are not statistically significant." (*See* Exhibit B of Colford Declaration at page 33 (or Exhibit B Page 12 of 33)).

The undersigned pointed out that the full name of the "DiaSorin" assay, as indicated in Colford Declaration, is INCSTAR N-tact PTH SP Intact PTH Kit." (*See* Colford Declaration, paragraph 3, at page 1.)

The Examiner and the undersigned then discussed the content of the LePage article. The undersigned pointed out that the LePage article contains comparative test data for three commercial two-site I-PTH assays: Allegro Intact PTH (Nichols Institute), N-tact PTH SP (Incstar), and Active Intact PTH (Diagnostic System Laboratories (DSL)). (*See* the LePage article at page 806, left column.) The undersigned also pointed out the comparative data shown in Figure 3 and the following statement in the LePage article:

> To gain a better understanding of these differences, we next analyzed the immunoreactivity of hPTH(1-84) and hPTH(7-84), a commercially available molecule potentially structurally related to the non-(1-84)PTH peak. As shown on Fig. 3, hPTH(1-84) and hPTH(7-84) reacted almost equimolarly in the Nichols assay, whereas hPTH(7-84) was only one-half as potent as hPTH(1-84) in the other two assays.

(*See* the LePage article at page 807, right column.) As indicated in the legend of Figure 3, the "other two assays" are the Incstar and DSL assays. Therefore, as shown in the LePage article, the Incstar assay has significant crossreactivity with hPTH(7-84).

The undersigned pointed out that Exhibit B of Colford Declaration shows that the Colford "(1-7)" assay correlates with the "DiaSorin" assay, which is the same as the Incstar assay tested in the LePage article, and the LePage article shows that the Incstar assay has significant crossreactivity with hPTH(7-84). The undersigned also pointed out that these data show that the Colford "(1-7)" antibody disclosed in the Colford 1997 Abstract and Presentation, even in view of Colford Declaration and Exhibit B of Colford Declaration, does not meet the limitation "avoids binding to a non-whole PTH fragment" of the present claims.

The Examiner indicated that he will consider Colford Declaration, its two Exhibits A and B, and the points raised by the undersigned.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and

authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 532212000623. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: February 26, 2008

Respectfully submitted,

By /Peng Chen/

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